DOCKET NO.: IBIS0002-100 (DIBIS-0003US) **PATENT**

REMARKS

Claims 51-68 are pending in the present application. Claims 51 and 67 have been amended herein. Upon entry of the present amendment, claims 51-68 will remain pending.

Claim 51 has been amended to recite that the "pair of primers hybridizes to nucleic acid of about one hundred or more bacterial species..." support for which can be found at, for example, page 13, lines 14-24 of the specification. No new matter has been added.

Claim 67 has been amended to recite that the variable region is "no more than about 60-100 nucleotides," support for which can be found, for example, at page 15, lines 2-9. No new matter has been added.

I. The Claimed Invention Is Not Obvious

Claims 51-68 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the combination of the following references: either 1) U.S. Patent No. 6,055,487 (hereinafter, the "Margery reference") or 2) U.S. Patent No. 6,018,713 (hereinafter, the "Coli reference") taken in view of either of 3) Muddimen et al., Anal. Chem., 1997, 69, 1543-1549 (hereinafter, the "Muddimann I reference") or 4) Muddimen et al., Anal. Chem., 1996, 68, 3705-3712 (hereinafter, the "Muddimann II reference"); taken in further view of Widjojoamodjo et al., J. Clin. Micro., 1994, 32, 3002-3007 (hereinafter, the "Widjojoamodjo reference"). Applicants traverse the rejection and respectfully request reconsideration because the combination of the cited references does not result in Applicants' claimed invention.

Claim 51, as amended herein, recites a service for providing bioagent characterizing information. A database of measured or calculated base compositions indexed to molecular masses of amplification products of nucleic acid of known bioagents is provided. These amplification products are obtained by amplification of bacterial nucleic acid with a pair of primers that hybridize to sequences of the bacterial nucleic acid. Each member of the pair of primers hybridizes to nucleic acid of about one hundred or more bacterial species. The sequences of the nucleic acid flank a variable nucleic acid sequence of the about one hundred or more bacterial species. The service also comprises interrogating the database with an identification query comprising a measured molecular mass of a bacterial bioagent. The measured molecular

mass is of a primer pair generated amplification product comprising a variable region that is present within a gene involved in translation, replication, recombination, repair, transcription, nucleotide metabolism, amino acid metabolism, lipid metabolism, energy generation, uptake, or secretion. The variable region is flanked by a pair of highly conserved regions to which the primer pair hybridizes. The service also comprises delivering a response generated by the database, wherein the response provides characterizing information for the bioagent.

None of the cited references, alone or in combination, teach or suggest a database that comprises measured or calculated base compositions indexed to molecular masses of amplification products of nucleic acid of known bioagents wherein the amplification products are obtained by amplification of bacterial nucleic acid with a pair of primers that hybridize to of about one hundred or more bacterial species sequences. Further, none of the cited references, alone or in combination, teach or suggest interrogating such a database with an identification query as presently recited in claim 51. Thus, the combination of the cited references does not produce Applicants' claimed invention.

In addition, Applicants traverse the rationale supplied in the present Office Action and the Office Action dated August 26, 2003 for combining the cited references. The position taken in the Office Actions is that it would have been obvious to perform "central laboratory testing for various medical issues including microbiology testing" (in view of the Margery and Coli references) and eliminate all microbiology testing procedures reported therein and replace them with the mass spectrometric methods (in view of the Muddiman I and II references) (see page 6 of the Office Action dated August 26, 2003). The Office also asserts that it would have been obvious to further "practice the conserved primer amplification via ribosomal rRNA sequence" (in view of the Widjojoamodjo reference) by eliminating the primers reported in either the Muddiman I or II references and replacing them with the primers of the Widjojoamodjo reference (see present Office Action at page 4).

In establishing a *prima facie* case of obviousness under 35 U.S.C. §103, it is incumbent upon the Examiner to provide a reason why one of ordinary skill in the art would have been led to modify a prior art reference or to combine reference teachings to arrive at the claimed invention. *Ex parte Clapp*, 227 U.S.P.Q. 972 (Bd. Pat. App. Int. 1985). To this end, the requisite

motivation must stem from some teaching, suggestion or inference in the prior art as a whole or from the knowledge generally available to one of ordinary skill in the art and not from appellants' disclosure, see for example, *Uniroyal Inc. v. Rudkin-Wiley Corp.*, 5 U.S.P.Q.2d 1434 (Fed. Cir. 1988); and *Ex parte Nesbit*, 25 U.S.P.Q.2d 1817, 1819 (Bd. Pat. App. Int. 1992). In this respect, the following quotation from *Ex parte Levengood*, 28 U.S.P.Q.2d 1300, 1302 (Pat. Off. Bd. App. 1993), is noteworthy:

> Our reviewing courts have often advised the Patent and Trademark Office that it can satisfy the burden of establishing a *prima facie* case of obviousness only by showing some objective teaching in either the prior art, or knowledge generally available to one of ordinary skill in the art, that "would lead" that individual "to combine the relevant teachings of the references." ... Accordingly, an examiner cannot establish obviousness by locating references which describe various aspects of a patent applicant's invention without also providing evidence of the motivating force that would **impel** one skilled in the art to do what the patent applicant has done. (citations omitted; emphasis added)

Significantly, the Office Action identifies no "motivating force" that would "**impel**" persons of ordinary skill to modify the respective teachings of the cited references and achieve the claimed invention.

There is no motivation to modify the computer-aided medical reporting systems of either the Margery or Coli references to produce Applicants' claimed service. In particular, there is no motivation to replace the "central laboratory testing" reported in Margery and/or Coli references with the mass spectrometry methods reported in the Muddiman I and/or II references. The Margery reference reports analytical devices for analyzing, for example, blood gases, pH, electrolytes, glucose, and hemoglobin. The Coli reference reports analytical devices for, for example, biochemical and microbiological testing (i.e., basic hematology, urinalysis, basic chemistry, special chemistry, and microbiology). These specific and generalized analytical procedures do not constitute the "impelling" motivation required under the law. Indeed, neither the Margery reference nor the Coli reference even suggest mass spectroscopy analysis of samples containing bioagents in order to identify any bioagents therein. It is only upon consideration of Applicants' disclosure that such an idea comes to mind. The fact that references can be found that report mass spectroscopy analysis of DNA, or any other feature recited in the pending claims, is

of no moment in considering motivation to modify a reported method. "A critical step in analyzing the patentability of claims pursuant to section 103(a) is casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field." *In re Kotzab*, 217 F.3d 1365, 1369, 55 U.S.P.Q.2d 1313, 1316 (Fed. Cir. 2000). "The invention must be viewed not with the blueprint drawn by the inventor, but in the state of the art that existed at the time." *In re Dembiczak*, 175 F.3d 994, 999, 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999) (quoting *Interconnect Planning Corp. v. Feil*, 774 F. 2d 1132, 1138, 227 U.S.P.Q. 543, 547 (Fed. Cir. 1985). To establish a *prima facie* case of obviousness, "there must be some teaching, suggestion or motivation in the prior art to make the specific combination that was made by the applicant." *In re Dance*, 160 F.3d 1339, 1343, 48 U.S.P.Q.2d 1635, 1637 (Fed. Cir. 1998). "In other words, the examiner must show reasons that the skilled artisan, confronted with he same problem as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed." *In re Rouffet*, 149 F.3d 1350, 1357, 47 U.S.P.Q.2d 1453, 1458 (Fed. Cir. 1998). Further, citing references which merely indicate that isolated elements and/or features recited in the claims are known is not sufficient basis for concluding that the combination of claimed elements would have been obvious. *Ex Parte Hiyamizu*, 10 U.S.P.Q.2d 1393 (Bd. Pat. App. Int. 1988).

The Office Action dated August 26, 2003 asserts that both the Margery and Coli references are directed to the "interactive ordering of testing at a central laboratory with computer network return of the test results" (see page 5). The Office Action further asserts that both references report "central laboratory testing inclusive of microbiology" (see page 5). The motivation for combining the Margery and/or Coli references with the Muddiman I and/or II references stated in the present Office Action is as follows:

> Said previously cited combination of references suggests and motivates identification wherever conserved primer amplification produces characteristic products for identification as is set forth in the art. An example of this motivation as generally applicable for identification is given in Muddiman et al. (1996), page 3712, in the CONCLUSIONS section wherein the 'general applicability of this approach' is stated in the first column, lines 12-14. Genetic variations are also suggested as

> determinable in Muddiman et al. (1996), page 3712, in the bridging sentence between the first and second columns. ["The application of this technique to screen for mutations should allow the accurate and rapid evaluation of genetic variations."] Different species of organisms are well known to correspond to genetic variations therein.

This alleged motivation, however, fails to even address why one skilled in the art would combine the Margery and/or Coli references with the Muddiman I and/or II references. Indeed, there is no discussion of any motivation to combine the service aspects of the Margery and/or Coli references with the mass spectrometry aspects of the Muddiman I and/or II references. One skilled in the art need not implement any aspects of the Margery and/or Coli references to identify bioagents. Further, the "general applicability of this approach" is quite far from the **impelling** motivation to which the Board of Appeals referred.

Thus, the claimed invention is not obvious in view of the combination of cited references. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §103(a) be withdrawn.

II. The Claims Are Clear And Definite

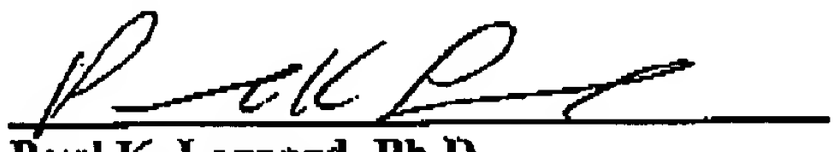
Claims 51-68 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. The Office Action asserts that it is unclear whether "generic bioagents are meant to be characterized which may include simple DNA, RNA, or possibly chemicals that may be utilized as bioagents" (see page 2). Although Applicants believe the claims are clear and definite as originally drafted, solely to advance prosecution of the present application, Applicants have amended claim 51 to recite "bacterial bioagent." Thus, the database is interrogated with an identification query comprising a measured molecular mass of a bacterial bioagent. The measured molecular mass is of a primer pair generated amplification product comprising a variable region that is present within a gene involved in translation, replication, recombination, repair, transcription, nucleotide metabolism, amino acid metabolism, lipid metabolism, energy generation, uptake, or secretion. Further, the variable region is flanked by a pair of highly conserved regions to which the primer pair hybridizes. Thus, a bacterial bioagent

(i.e., a bacterium) that contains a nucleic acid sequence to which the primer pair hybridizes (and thus, an amplification product can be obtained) can be identified based upon the molecular mass of the resultant amplification product. Persons of ordinary skill would have no difficulty in determining whether a particular service meets the criteria recited in the claims. Accordingly, the claims are definite within the meaning of §112. In re Mercier, 185 U.S.P.Q. 774 (C.C.P.A. 1975) (claims sufficiently define an invention so long as one skilled in the art can determine what subject matter is or is not within the scope of the claims). Thus, claims 51-68 are clear and definite. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §112, second paragraph be withdrawn.

III. Conclusion

Applicants submit that the pending claims are in condition for allowance. Applicants respectfully request that the Examiner contact Applicants' undersigned representative if such allowance is not forthcoming.

Respectfully submitted,



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